

# REQUEST FOR ACCESS OF ABANDONED APPLICATION UNDER 37 CFR 1.14(a)

RECEIVED

MAY 23 2001

File Information Unit

In re Application of

Application Number

07/310252

Filed

2/13/89

Group Art Unit

Examiner

Paper No.

#29

Assistant Commissioner for Patents  
Washington, DC 20231

I hereby request access under 37 CFR 1.14(a)(3)(iv) to the application file record of the above-identified ABANDONED application, which is: (CHECK ONE):

\_\_\_ (A) referred to in United States Patent Number 5693762, column \_\_\_\_\_

\_\_\_ (B) referred to in an application that is open to public inspection as set forth in 37 CFR 1.11, i.e., Application No. \_\_\_\_\_, filed \_\_\_\_\_, on page \_\_\_\_\_ of paper number \_\_\_\_\_

\_\_\_ (C) an application that claims the benefit of the filing date of an application that is open to public inspection, i.e., Application No. \_\_\_\_\_, filed \_\_\_\_\_, or

\_\_\_ (D) an application in which the applicant has filed an authorization to lay open the complete application to the public.

Please direct any correspondence concerning this request to the following address:

\_\_\_\_\_  
\_\_\_\_\_  
\_\_\_\_\_

Thomas L. Hazel

Signature

5/23/01  
Date

Thomas L. Hazel

Typed or printed name

FOR PTO USE ONLY

Approved by:

(initials)

Unit:



US005693762A

**United States Patent** [19]

Queen et al.

[11] Patent Number: 5,693,762

[45] Date of Patent: Dec. 2, 1997

## [54] HUMANIZED IMMUNOGLOBULINS

[75] Inventors: Cary L. Queen, Los Altos; Man Sung Co, Cupertino; William P. Schneider, Mountain View; Nicholas F. Landolfi, Milpitas; Kathleen L. Coelingh, San Francisco; Harold E. Selick, Belmont, all of Calif.

[73] Assignee: Protein Design Labs, Inc., Mountain View, Calif.

[21] Appl. No.: 487,200

[22] Filed: Jun. 7, 1995

**Related U.S. Application Data**

[63] Continuation of Ser. No. 634,278, Dec. 19, 1990, Pat. No. 5,530,101, which is a continuation-in-part of Ser. No. 590,274, Sep. 28, 1990, abandoned, and Ser. No. 310,252, Feb. 13, 1989, abandoned, which is a continuation-in-part of Ser. No. 290,975, Dec. 28, 1988, abandoned.

[51] Int. Cl.<sup>6</sup> ..... A61K 39/395

[52] U.S. Cl. .... 530/387.3; 530/388.22; 424/133.1; 424/143.1

[58] Field of Search ..... 530/387.3, 388.22; 424/133.1, 143.1

[56] **References Cited****U.S. PATENT DOCUMENTS**

4,578,335	3/1986	Urdal et al.	530/351
4,816,397	3/1989	Boss et al.	435/68
4,816,565	3/1989	Honjo et al.	435/69.1
4,816,567	3/1989	Cabilly et al.	530/387
4,845,198	7/1989	Urdal et al.	530/387
4,867,973	9/1989	Goers et al.	424/85.91
5,198,359	3/1993	Taniguchi et al.	435/252.3
5,225,539	7/1993	Winter	530/387.3
5,476,786	12/1995	Huston et al.	435/252.33

**FOREIGN PATENT DOCUMENTS**

0 120 694	10/1984	European Pat. Off.
0171496	2/1986	European Pat. Off.
0173494	3/1986	European Pat. Off.
0184187	6/1986	European Pat. Off.
0256654	7/1987	European Pat. Off.
0 239 400	9/1987	European Pat. Off.
0239400	9/1987	European Pat. Off.
0266663	6/1988	European Pat. Off.
0 323 806	7/1989	European Pat. Off.
0 328 404	8/1989	European Pat. Off.
0 365 209	4/1990	European Pat. Off.
0 365 997	5/1990	European Pat. Off.
0 125 023	6/1991	European Pat. Off.
0460167	12/1991	European Pat. Off.
2188941	10/1987	United Kingdom
8928874	12/1989	United Kingdom
WO 86/05513	9/1986	WIPO
WO 87/02671	5/1987	WIPO
WO 88/09344	12/1988	WIPO
WO 89/01783	3/1989	WIPO
91/09967	7/1991	WIPO

**OTHER PUBLICATIONS**

Groves et al. *Hybridoma* vol. 6 (1) 1987 71.  
 Chothia, C. and Lesk, A.M., "Canonical Structures for the Hypervariable Regions of Immunoglobulins," *J. Mol. Biol.*, 196:901-917 (1987).  
 Jones et al., "Replacing the complementarity-determining regions in a human antibody with those from a mouse," *Nature*, 321:522-525 (1986).  
 Junghans et al., *Cancer Res.*, 50:1495-1502 (1990).  
 Kupiec-Weglinski et al., *Proc. Natl. Acad. Sci.*, 83:2624 (1986).  
 Maeda et al., "Construction of reshaped human antibodies with HIV-neutralizing activity," *Hum. Antibod. Hybrid.*, 2:124-134 (1991).  
 Morrison et al., "Chimeric human antibody molecules: Mouse antigen binding-domains with human constant region domains," *Proc. Natl. Acad. Sci.*, 81:6851-6859 (1984).  
 Morrison, S.L., "Transfectomas Provide Novel Chimeric Antibodies," *Science*, 229:1202-1207 (1985).  
 Neuberger et al., "A hapten-specific chimeric IgE antibody with human physiological effector function," *Nature*, 314:268-270 (1985).  
 Riechmann et al., "Reshaping human antibodies for therapy," *Nature*, 332:323-327 (1988).  
 Sahagan et al., "A Genetically Engineered Murine/Human Chimeric Antibody Retains Specificity for Human Tumor-Associated Antigen," *J. Immunol.*, 137:1066-1074 (1986).  
 Verhoeyen et al., "Reshaping Human Antibodies: Grafting an Antilysozyme Activity," *Science*, 239:1534-1536 (1988).  
 Amit et al., *Science*, 233, 747-753 (1986).  
 Cheetham, *Protein Engineering*, 2(3), 170-172 (1988).

(List continued on next page.)

Primary Examiner—Lila Feisee

Assistant Examiner—Julie E. Reeves

Attorney, Agent, or Firm—Townsend &amp; Townsend &amp; Crew

[57] **ABSTRACT**

Novel methods for producing, and compositions of, humanized immunoglobulins having one or more complementarity determining regions (CDR's) and possible additional amino acids from a donor immunoglobulin and a framework region from an accepting human immunoglobulin are provided. Each humanized immunoglobulin chain will usually comprise, in addition to the CDR's, amino acids from the donor immunoglobulin framework that are, e.g., capable of interacting with the CDR's to effect binding affinity, such as one or more amino acids which are immediately adjacent to a CDR in the donor immunoglobulin or those within about 3 Å as predicted by molecular modeling. The heavy and light chains may each be designed by using any one or all of various position criteria. When combined into an intact antibody, the humanized immunoglobulins of the present invention will be substantially non-immunogenic in humans and retain substantially the same affinity as the donor immunoglobulin to the antigen, such as a protein or other compound containing an epitope.

20 Claims, 55 Drawing Sheets